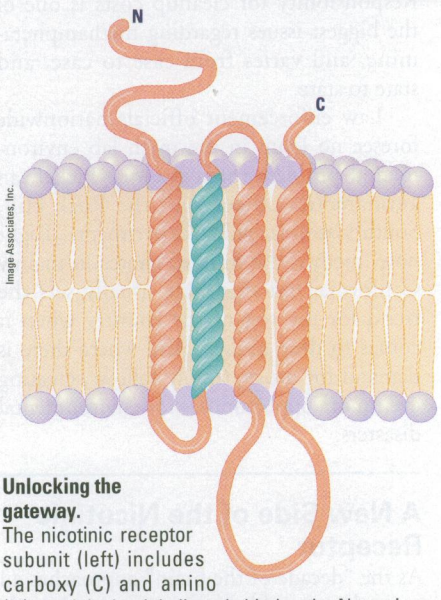
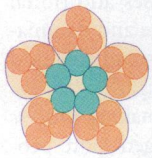


Unlocking the gateway.
The nicotinic receptor subunit (left) includes carboxy (C) and amino (N) termini; nicotinic ligands bind to the N terminus. The complete channel is thought to comprise five subunits clustered around a central ion "passageway" (right) that opens and closes like a camera shutter.

build upon that work by determining whether the nicotinic receptor would exhibit characteristics similar to those of the serotonin receptor. The scientists made an important discovery: nicotinic receptors, which had previously been thought to exist only on the presynaptic terminals of excitatory cells in the hippocampus, were also found on interneuronal (probably inhibitory) cells. The nicotinic receptor was thus found to act in a way previously unsuspected, possibly suggesting a novel mechanism by which acetylcholine may regulate neuronal activity in the hippocampus. This may further indicate that nicotinic ligands—the substances that bind to the nicotinic receptor—could be used as preventive measures against diseases associated with functions regulated by the receptor.

Neurological disease is a mysterious realm, with scientists' understanding limited to a few tantalizing bits of knowledge. It is known, for instance, that a mutation in one of the subunits of the nicotinic receptor is associated with the rare autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), although whether this particular mutation actually causes this form of epilepsy has not been conclusively shown. It is also known that Alzheimer's patients have fewer nicotinic receptors in their cerebral cortex, the portion of the brain that is ravaged by the irreversible disease. But the relationships between the various components that make up the electrical circuit that powers the brain are largely undefined. Scientists such as Yakel and Jones are beginning to look at more specialized groups of cells in order to tease apart these relationships.

Theoretically, Yakel says, the ligands that bind with the nicotinic receptor could be used to treat diseases such as Alzheimer's disease. Nicotine has been observed to improve memory, including that of some Alzheimer's patients. Little is known, though, about how nicotine actually works in the brain.



Some Alzheimer's patients are currently treated with a drug called tacrine that works by blocking the enzyme acetylcholinesterase, which breaks down acetylcholine, therefore prolonging the period of time that neurons are exposed to the neurotransmitter. While the cellular activity of the drug appears clear, it is uncertain exactly why or how the drug works, and to what degree the nicotinic receptor is involved. Yakel says that further work with the nicotinic receptor will focus on ascertaining whether it has a direct link with Alzheimer's disease.

EDF Launches "3,000 by 2000" Project

Last year, the Environmental Defense Fund (EDF) released a study called *Toxic Ignorance* that found that the U.S. public does not have access to data on the basic health effects of 71% of high production volume chemicals. High production volume chemicals are defined by the EPA as those that are imported into or produced in the United States annually in quantities greater than 1 million pounds.

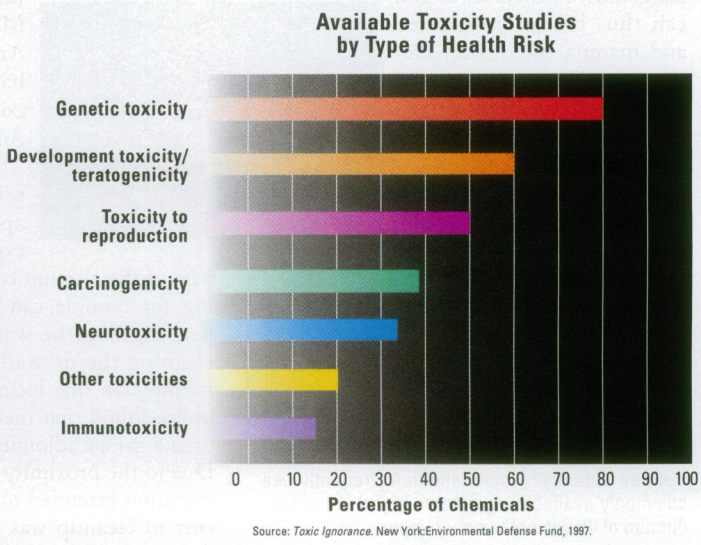
According to the Toxic Substances Control Act (TSCA) of 1976, the responsibility for testing chemicals for effects on health and the environment lies with the manufacturers of the chemicals. However, the EDF study asserts, up to this point, few efforts have been made by the chemical manufacturers to comply, and the government has not been effective in enforcing the mandates of the act. The EDF study states that this is due to the "self-defeating" language and structure of the TSCA, which cause it to be vulnerable to legal attacks by chemical manufacturers, thereby foiling the EPA's efforts to require chemical testing.

The EDF has begun a campaign to contact the chemical manufacturers directly, and challenge them to take responsibility and commit to testing chemicals. The goal of the campaign, called "3,000 by 2000," is to have health effects data available to the public for the top 3,000 high production volume chemicals by the year 2000.

The EDF sent letters to the top 100 chemical producers and challenged them to commit to completing a preliminary health screening on all chemicals that are produced in excess of 10 million pounds per year by 1 March 1999, and to screen all chemicals produced in excess of 1 million pounds per year by 1 January 2000. The EDF requested that the chemical manufacturers perform tests based on the human health hazard elements of the Screening Information Data Set (SIDS), developed in 1990 by the international Organisation for Economic Co-operation and Development (OECD) and the chemical manufacturing industry. SIDS is now considered the international standard for chemical testing. The six categories of potential adverse human health impacts are acute toxicity, repeated dose toxicity, *in vitro* genetic toxicity, *in vivo* genetic toxicity, developmental toxicity (including teratogenicity), and reproductive toxicity.

Eleven companies agreed to comply with the EDF's request, while six refused. Many others cited their current efforts to test chemicals. The EDF placed an advertisement in the 3 December 1997 issue of *USA Today* listing the companies that committed to the project, as well as those that refused.

By widely publicizing the campaign, the EDF has thrust the issue of chemical testing into the international spotlight,



Source: *Toxic Ignorance*. New York:Environmental Defense Fund, 1997.

helping it gain priority with government and industry groups. Thus far, response to the campaign has been generally positive, with government agencies and industry agreeing on the importance of the issue and cooperating to determine what steps need to be taken to test chemicals and make the data available to the public.

The Chemical Manufacturers Association (CMA), an industry organization that represents most of the 100 companies that were contacted by the EDF, has been active in discussions with the EDF and the EPA. The EDF actions were "favorably received," says Mort Mullins, vice president for regulatory affairs at the CMA. "We agreed with EDF that progress toward getting the OECD/SIDS data [on the chemicals] has not been achieved."

However, Mullins says that a CMA study conducted after the EDF released its findings indicates that there are data available for 47% of the chemicals, rather than the 29% that the EDF found. The CMA included information in its study that was not accessible by the EDF because certain databases containing such information are not currently available to the public.

Mullins says the CMA is conducting another in-depth audit of its databases to determine what chemicals have been tested. The group will then determine which steps need to be taken to compile existing information and put it into a format that will be accessible by the public. For chemicals that have not been tested for health effects, the CMA plans to oversee a testing process, divvying up the chemicals between different companies, Mullins says.

The EPA has also been auditing its databases to determine what data are available. Once chemicals that need to be tested have been identified, the EPA will work to ensure that they are tested, perhaps through regulation. "We have the authority under TSCA to require testing," says Charlie Auer, director of the chemical control division of the EPA. "We haven't written a rule, but we've been thinking about that. In the past, we've relied on voluntary efforts by companies. The problem in the U.S. is that we need to get more companies involved. One way to do that is through regulation."

Meanwhile, the OECD is examining the issue from a global perspective. So far, there has been a lot of action in a short period of time. "The key is going to be to go from the talk stage to the action stage," says David Roe, senior attorney for the EDF. He says the EDF plans to serve as a watchdog on the issue, adding, "We're in it for the long haul."

EHPnet

Doing a World of Good

Cooperation is crucial to meeting the environmental, resource, and development challenges of global significance for the future. The World Resources Institute (WRI) is an independent center dedicated to working with governments and private organizations to face these challenges.

The mission of the WRI, which celebrated its 15-year anniversary last year, is to teach and inspire human society to live in ways that protect the earth's environment and its capacity to provide for the needs and aspirations of current and future generations. The WRI conducts policy research and technical assistance on global environmental and development issues.

The WRI is accessible on-line through its site located at http://www.wri.org. The home page contains links that provide general information about the WRI, as well as information about its programs.

WORLD RESOURCES INSTITUTE

A link to Business and Technology provides information about two programs through which the WRI is working with industry on environmental issues. The WRI's Program in Technology and the Environment works with industry to develop environmentally efficient technologies, while the Management Institute for Environment and Business (MEB) works with universities, graduate schools, and corporations to integrate environmental issues into their educational programs. A link to the Business–Environment Learning and Leadership Program (BELL) tells how the MEB works with professors to enhance curricula, host seminars and conferences, and develop partnerships between universities and communities.

Another WRI program that works to involve businesses in environmental issues is the Climate Protection Initiative. Through this program, the WRI partners with businesses to identify "safe, climate-sound" government policies and corporate strategies. The What's New link on the home page offers an example of a partnership—the "Safe Climate, Sound Business" project—which is described under the WRI and General Motors Dialogue on Climate Change link. This collaboration between the WRI and General Motors will identify ways to reduce greenhouse gas emissions while protecting the economy.

The WRI also has an active division that works to protect human health, called the Program in Health, Environment, and Development (HED), which can be found via the Health and Environment link on the home page. HED investigates the impact of factors such as climate change and pollution on human health and seeks to develop policies to reduce human risk. Found on the HED page is information about a report, *The Hidden Benefits of Climate Policy: Reducing Fossil Fuel Use Saves Lives Now*, which is the first study to look at the global short-term health impact of fossil fuel consumption projects. The study says that by implementing climate policies now, approximately 8 million deaths resulting from particulate air pollution and the buildup of greenhouse gases could be avoided in the next two decades.

The WRI is also active in education through the Environmental Education Project, which is found under the link to Environment and Education. This program works with educational groups in the United States, Mexico, India, Europe, Australia, Vietnam, and Japan to develop and implement teaching materials about the environment including videos, teachers' guides, slide presentation sets, and computer software.

Information about programs in Africa and Asia can be found via links to the Policy Consultative Group for Africa and the Resources Policy Support Initiative, which works with Southeast Asia. These groups supply information about sustainable development and management of natural resources. The Forest Resources link provides information about the Forest Frontiers Initiative (FFI), a project that works to promote stewardship of forests. From this page, a link to Frontier News provides information such as news stories and statistics about forests around the world. A link from the FFI page to Business News contains information about another business/WRI partnership called the MacArthur Foundation–MEB/WRI Forestry Project, which works to expand the number of companies engaged in sustainable forestry, and to increase investment in sustainable forestry.

Other links from the WRI home page provide comprehensive information about issues such as biodiversity, sustainable agriculture, climate change, and global warming.